Fontham, E.T.H., Correa, P., Reynolds, P., Wu-Williams, A., Buffler, P.A., Greenberg, R.S., Chen, V.W., Alterman, T., Boyd, P., Austin, D.F., and Liff, J., "Environmental Tobacco Smoke and Lung Cancer in Nonsmoking Women: A Multicenter Study," Journal of the American Medical Association 271(22): 1752-1759, 1994

- This paper reports on the completion of a multicenter case-control study on ETS and lung cancer in female nonsmokers first reported in 1991. It includes 653 histologically confirmed lung cancer cases and 1253 controls.

- For spousal smoking and lung cancer in female nonsmokers, the authors report statistically significant risk estimates: a "crude" risk estimate of 1.26 (95% CI 1.04-1.54), and an adjusted risk estimate of 1.29 (95% CI 1.04-1.30). These contrast with the spousal smoking risk estimate from the initial study, which was not statistically significant.

- The reported overall workplace risk estimate is 1.12 (95% CI 0.91-1.38), and 1.39 (95% CI 1.11-1.74) after adjustment. To put this in perspective, of 18 workplace risk estimates for nonsmoker lung cancer reported in the literature, the vast majority (16 of 18) are not statistically significant.

- For social exposures, the authors report statistically significant risk estimates, e.g., an adjusted risk estimate of 1.50 (95% CI 1.19-1.89). These contrast with risk estimates reported in other studies for exposure in social and other settings which have not been statistically significant.

- The authors report risk estimates that are not statistically significant for childhood exposure and adult lung cancer. The reported findings are in accord with the majority of studies on childhood exposures. However, for women reporting both childhood exposure and the highest level of adult exposure, Fontham, et al., report a statistically significant risk estimate of 3.25 (95% CI 2.42-7.46).

- Despite their use of cotinine to assess current tobacco use, the authors acknowledge that misclassification of ever smokers as lifetime never smokers is "problematic" because there is "no biomarker of lifetime tobacco use."

- In this study, as in all spousal smoking studies, exposure was assessed via questionnaire. Study participants, 90% of whom were over 50 years old, were asked to recall exposures to ETS both from adulthood and from childhood. No actual ETS measurements were taken.

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- The authors claim that neither fruit, vegetable and vitamin consumption, nor dietary cholesterol were confounders for the reported ETS-lung cancer association. However, they apparently did not consider dietary saturated fat intake in their analyses. A recent study from the National Cancer Institute, by Alavanja, et al., reported that high saturated fat consumption was associated with a statistically significant increased risk of lung cancer, independent of any exposure to ETS.

- The socioeconomic and educational composition of the study population is not representative of the U.S. population as a whole. Almost half the cases (42%) and more than a third of the controls (38%) reported an annual household income of less than $20,000 per year; 29% of cases and 24% of controls had an income of less than $13,000 per year. Moreover, two-thirds of the cases and over half the controls had no more than a high school education.

- More than 100 case-control groupings were investigated. This is a clear case of "data-dredging." With so many statistical evaluations, it is likely that some of the reported statistically significant associations may have arisen by chance.

- Despite its relatively large size, the study sample of 653 cases was subdivided in order to present a large number of subgroup analyses. Thus, a number of the reported statistically significant associations are <u>not</u> based on the complete sample. Some of the subgroups consist of less than 100 cases.

- Despite the study's multicenter design, more than 80% of the cases and controls came from Los Angeles or San Francisco, California. Outdoor air pollution, which has been suggested to be a risk factor for lung cancer, was apparently not considered in this study.

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